

DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH

Fiscal Year 2014 Budget Request

Statement for the Record

Senate Subcommittee on Labor-HHS-Education Appropriations

Story C. Landis, Ph.D., Director
National Institute of Neurological Disorders and Stroke

May 2013

Mr. Chairman and Members of the Committee:

I am pleased to present the President's Budget request for the National Institute of Neurological Disorders and Stroke (NINDS) of the National Institutes of Health (NIH). The fiscal year (FY) 2014 NINDS budget of \$1,642,619,000 includes an increase of \$19,275,000 over the comparable FY 2012 level of \$1,623,344,000.

COMBATING NEUROLOGICAL DISORDERS

The NINDS mission is to reduce the burden of neurological disorders through research. For stroke, research on prevention and treatment led to reductions of the age-adjusted death rate by 36.9 percent and of the actual number of deaths by 22.9 percent from 1999 to 2009¹.

An intensive and inclusive NINDS planning process has identified the highest priority research investments to continue this progress against stroke. Experts across disciplines agreed that stroke clinical trials networks could accelerate progress. In response, NINDS is establishing a flexible stroke clinical trials network to conduct prevention, treatment, and recovery trials. With shared infrastructure, the network will better set priorities for studies, reduce cost and time in start-up, and therefore significantly improve efficiency. The network builds on lessons from the NeuroNEXT network, which expedites early phase clinical trials of new treatments, especially for rare diseases. NeuroNEXT uses a single Institutional Review Board and standard site contracts, which reduce time required to start a trial by months. It also accommodates projects from academic investigators or private partners. Trials for spinal muscular

¹ Circulation 134:e6-245, 2013

atrophy (SMA) biomarkers and secondary progressive multiple sclerosis are under way, and planning has begun for clinical trials of two therapies developed by the NIH Therapeutics for Rare and Neglected Disease Program.

Reducing cognitive impairment from brain vascular disease is another priority that emerged from planning. Stroke itself is a major cause of dementia. Furthermore, the 7 million U.S. stroke survivors have an increased likelihood of cognitive problems, and the 13 million people with “silent strokes”² may also be at risk. Vascular risk factors are also associated with Alzheimer’s disease. In fact, there is a spectrum from pure vascular dementia to pure Alzheimer’s disease, with most patients having contributions from both³. This month a scientific workshop on Alzheimer’s Related Dementias, part of the National Alzheimer’s Project Act activities, focused on vascular dementia.

Traumatic Brain Injury (TBI) is the leading cause of death and disability in children and young adults, common among the elderly, and a major concern for the military and veterans. New studies will address two reasons why more than 30 major clinical trials of interventions for TBI failed to demonstrate improved outcomes: classification schemes do not distinguish between different types of damage in different parts of brain that may respond differently to interventions, and large variations in outcomes among medical centers confound assessment of interventions in clinical trials. A study of 1,000 children will evaluate the effectiveness of six major critical care guidelines for severe, pediatric TBI that lack compelling evidence. Another prospective, observational, multi-center study of 5,000 adults and children with TBI will

² Circulation 125:e2-e220, 2012

³ Neurology 72:368-74,2009

be coordinated with studies by the European Union and the Canadian Institute of Health Research to enhance the statistical power to detect differences. The research community has agreed upon standards through the NINDS TBI Common Data Elements program that will allow meaningful comparison across studies, and the Department of Defense and NIH-led Federal Interagency TBI Research informatics system (FITBIR) provides a database for sharing information. NIH is also addressing TBI through the Foundation for NIH's Sports and Health Research Program, with support from the National Football League. In December a workshop focused on Chronic Traumatic Encephalopathy (CTE), a neurodegenerative disorder that can follow repetitive mild brain trauma in sports and the military. Follow-up research solicitations are underway, and this public private partnership will address other key aspects of sports and health in the coming years.

Epilepsy is another common disorder that affects people of all ages. Every six years since 2001, the Epilepsy Benchmarks process has brought NINDS, the research community, and non-governmental organizations together to establish research milestones and monitor progress. This April NINDS convened a major workshop to assess progress and set pathways forward. Previous Benchmarks guided investments that are now yielding important gene findings, advances in understanding how epilepsy develops, and attention to comorbidities, including Sudden Unexplained Death in Epilepsy (SUDEP). Future Benchmarks will focus on disease progression and modification, predictability of seizures and treatment response, and aspects of gender, ethnicity, and age (children and elderly), among other issues. Opportunities from other investments could also have a significant impact on epilepsy. The community is

excited, for example, about advances in genetics, “big data,” and brain circuit analysis.

Opportunities are also emerging for many other brain diseases, common and rare. Induced pluripotent stem cells derived from patients with Parkinson’s disease, amyotrophic lateral sclerosis (ALS), Huntington’s and other disorders allow laboratory testing of potential drugs. Biomarkers under development for Parkinson’s, SMA, and other diseases will speed clinical testing. Brain stimulation therapies have proven benefit for Parkinson’s disease, essential tremor, and dystonia, and show promise for diseases including epilepsy and Tourette syndrome. In research settings, brain machine interfaces enable paralyzed individuals to control a robotic arm and hand; development of practical devices is underway. Gene discoveries have led to mechanism targeted therapies that are now in the translational pipeline for many diseases, for example, muscular dystrophies, SMA, familial dysautonomia, and fragile X.

BASIC NEUROSCIENCE

Researchers in academia and industry agree that basic science drives progress against disease. A few recent examples: genes discovered for epilepsy, ALS, and autism enable the dissection of underlying disease mechanisms, pointing to potential targets for therapy development. Research is also revealing unexpected ways that degeneration propagates in the brain, why acute pain can become chronic, and that serious disabilities in children born prematurely may be more reversible than expected. Science of the normal brain advanced this year on topics as diverse as the mechanisms of itch, how the brain clears waste, control of brain blood flow in infants, the influence of anesthetics on consciousness, and brain circuits for memory.

NINDS relies on investigator-initiated research throughout its programs. Engaging the insight and ingenuity of the scientific community in this way is especially crucial for basic research. The Institute has also emphasized the importance of transparent reporting of research findings, stressing rigor and reproducibility. A June 2012 NINDS workshop brought together representatives of all major stakeholders, which has already lead to changes within and outside the NIH, including policies of leading journals⁴.

Technology can also empower investigators. Investment by the NIH and others, together with advances in optics, computer science, genetic engineering, and other disciplines, has led to promising technological strategies to study the activity of large numbers of brain cells and the intricacies of their connections. The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative partners federal agencies and private foundations in a coordinated program to develop and apply these emerging opportunities, including study of the human brain. This will ultimately revolutionize understanding of how networks of brain cells enable us to perceive, think, and act, and what goes wrong in diseases of the brain. A stellar committee of scientists will guide this initiative, with recommendations on first steps due this fall and a more complete plan the following summer. History suggests that the most important benefits of BRAIN will be those that we have not yet even imagined.

⁴ e.g., [Nature](#) 490:187-91,2012; [Nature](#) 496: 398, 2013; [Nature Neuroscience](#) 16:1, 2013; 16:517, 2013

Story C. Landis, Ph.D.

Director, National Institute of Neurological Disorders and Stroke

Dr. Story C. Landis began her appointment as the Director of the National Institute of Neurological Disorders and Stroke (NINDS) on September 1, 2003. A native of New England, Dr. Landis was awarded her B.A. degree in Biology, with highest honors, from Wellesley College (1967), and her M.A. (1970) and Ph.D. (1973) degrees from Harvard University. After postdoctoral work at Harvard University studying transmitter plasticity in sympathetic neurons, she served on the faculty of the Harvard Medical School's Department of Neurobiology.

In 1985, Dr. Landis joined the faculty of the Case Western Reserve University School (CWRU) of Medicine in Cleveland, Ohio, where she held many academic positions, including Professor and Director of the Center on Neurosciences, and Professor and Chairman of the Department of Neurosciences, a department that she was instrumental in establishing. Under her leadership, the CWRU Department of Neurosciences achieved worldwide acclaim and a reputation for excellence. In 1995, Dr. Landis was appointed as the NINDS Scientific Director, and was responsible for the direction and re-engineering of the Institute's intramural research program. Beginning in 1999, in conjunction with the leadership of the National Institute of Mental Health (NIMH), she spearheaded a movement to bring a sense of unity and common purpose to the numerous laboratories, in multiple NIH Institutes that conduct leading edge clinical and basic neuroscience research. This increased research cooperation and collaboration, and resulted in the construction of the new NIH Neuroscience Research Center, Phase

II, on the NIH campus. Since early 2007, Dr. Landis has also been Chair of the NIH Stem Cell Task Force.

Throughout her research career, Dr. Landis has made many fundamental contributions to understanding the developmental interactions required for synapse formation, and has garnered many honors and awards. Dr. Landis is an elected Fellow of the American Academy of Arts and Sciences and the American Association for the Advancement of Science, and an elected member of the American Neurological Association. In 2002, she was elected President of the Society for Neuroscience, and served as President-elect until her appointment as the NINDS Director in September 2003. In 2009, Dr. Landis was elected to the Institute of Medicine of the National Academy of Sciences.